DETAILED ACTION

Response to Arguments

Applicants have presented arguments and Declarations by Chris Rundfelt and Wolfgang Loscher, each of which will be addressed. Applicants again point to the previous response and Declarations that the conclusion of the Loscher reference was misstated. The Examiner stated that Loscher concludes that the epileptic dog is indeed a suitable model of human epilepsy. Applicants argue that the Declarations provide evidence that the pharmacokinetics of the standard drugs do not permit maintenance of effective drug levels in the dog. Applicants then refer to the enclosed Declarations, which will be addressed individually below.

In response to Applicants arguments, it is once again pointed out that the rejections were not made based on AWD 131-138 being effective in humans and therefore making the presumption that it will be effective in dogs. The references used in the rejection were made to teach that AWD 131-138 were tested in animal models of idiopathic epilepsy (Bialer) and two references were utilized to define the different types of epilepsy and to conclude that Bialer teaches idiopathic epilepsy.

Applicants have attempted to clear up the reason for the Rostock reference. Applicants assert that Rostock used mice and rats with induced epilepsy to establish an extrapolation between what is efficacious in rodent models and humans. Applicants make this point to argue that the degree one may extrapolate between rodent models and humans, such extrapolations cannot be carried over to dogs. Applicants further argue that the references used by the Examiner to support the interpretation of

idiopathic epilepsy are distinguished from the induced epilepsy rodent models taught in the prior art used by the Examiner. Applicants argue that one would not select a drug useful in petit-mal seizures because they are not found in dogs, rather one would look for a drug effective on tonic-clonic convulsions which is not taught by the cited references. Applicants discuss the WAG model as not being a form of idiopathic epilepsy in dogs. Applicants assert that the combination of Ross and French with Bialer is not proper because the references discuss induced epilepsy in rodent and human epilepsy, both of which Applicants assert is not the same as epilepsy in dogs.

As discussed above, the rejections were not based on an extrapolation of rat data to the human condition in regards to the Rostock reference. It is pointed out that Bialer teaches that AWD 131-138 has broad spectrum anticonvulsant activity and exerts anticonvulsant activity at doses below those inducing motor impairment in rats and dogs. Because Bialer teaches that AWD 131-138 is useful in both rodents and canines, and different forms of epilepsy, it would be obvious to try AWD 131-138 in different dog models of epilepsy, including idiopathic epilepsy. Further, the rejection relates tonic-clonic seizures to idiopathic epilepsy as discussed below.

The Declaration of Chris Rundfeldt outlines experiments in dogs and rats with AWD 131-138, in addition to two other compounds with similar structures, AWD 131-139 and AWD 131-175. Experiments show that all three compounds were more effective in rodent models of induced seizures; however, this result could not be extrapolated to dogs because AWD 131-139 and AWD 131-175 rapidly degraded in the dog.

While the above arguments are appreciated, it is noted that the rejection was made on the same premise of this study. Bialer teaches that AWD 131-138 has been developed because of its broad spectrum of anticonvulsant activity and that it exerts anticonvulsant activities at doses clearly below those inducing motor impairment in rat and dog seizure models. As discussed in the rejection, AWD 131-138 is tested in both rat and dog seizure models and points out some seizure models in rats that are idiopathic in nature. Considering that the teachings of Bialer focus on treatment of AWD 131-138 in dogs and rats, and teach that AWD 131-138 is effective in idiopathic type seizures in rats, it would be obvious to try treating dogs with AWD 131-138 in idiopathic seizures. The results of the Declaration are understood that the activity of drugs may not necessarily be the same between rodents and canines; however, Bialer clearly shows that AWD 131-138 is active in both rodents and canines.

The Declaration of Wolfgang Loscher has been fully considered. In particular, it is argued that there are similarities between canine epilepsy and human epilepsy but this can not be generalized to the treatment of epilepsy. It is argued that at least one difference between canines and humans is that dogs do not have petit mal seizures. Loscher goes on to discuss that treating the epileptic dog can only be a model of human epilepsy in certain instances. Loscher argues that dogs have a high metabolizing capacity and therefore drugs that are effective in humans may not be in dogs because of this.

While the above arguments are appreciated, it should be noted that the rejection was not based on the assumption that treatments that are effective in humans will

extrapolate to dogs. The rejection was based on treating dogs with AWD 131-138. The description of the types of seizures by Ross et al. and French were used only to define the different types of epilepsy.

Claim Rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 12-15, 19 and 22 rejected under 35 U.S.C. 103(a) as being unpatentable over Bialer et al. (J Epilepsy Research (Jan 2001) 43, pgs. 11-58) in view of Ross et al. (Neurosci Biobehav Rev, 24 (2000) 639-653) and French (Am J Managed Care, Vol. 7, No. 7, 2001).

Bialer et al. teach that AWD 131-138 treats audiogenic clonic seizures and absence epilepsy in genetic models of epilepsy (meeting the limitation of claim 12; pg. 12, Section 2.1.1.1). Because it is taught that AWD 131-138 has anticonvulsant activities in animal models of epilepsy, it is obviously taught that AWD 131-138 would effectively treat epilepsy regardless of when it was diagnosed (meeting the limitation of claim 19). Though Bialer et al. does not teach the treatment of dogs with AWD 131-138 in the AGS model or in absence epilepsy, the treatment of dogs is taught in other models. Therefore, there would be a reasonable expectation of success that AWD 131-

138 would be an effective treatment for idiopathic epilepsies. Bialer also teaches that repeated administration shows no evidence of tolerance, indicating that chronic administration would be indicated for a chronic idiopathic epileptic condition.

Bialer et al. does not specifically state that the forms of epilepsies are idiopathic.

Ross et al. teach that AGS is a form of epilepsy associated with generalized seizure displayed by clonic or tonic-clonic seizure activity (see first paragraph of Introduction).

French teaches that clonic or tonic-clonic seizure activity is a form of idiopathic epilepsy (see Role of New AEDs on page S209).

Because Ross et al. and French teach that AGS is a form of idiopathic epilepsy, it would be obvious to a person of ordinary skill in the art at the time of the invention that Bialer et al. is teaching the treatment of different forms of idiopathic epilepsy with AWD 131-138. Though Bialer et al. does not teach the treatment of dogs with AWD 131-138 in the AGS epilepsy model or in absence epilepsy animals, the treatment of dogs is taught in other models. Therefore, there would be a reasonable expectation of success that AWD 131-138 would be an effective treatment for idiopathic epilepsies. One would be motivated to treat idiopathic epilepsy with AWD 131-138 with a reasonable expectation of success because it is taught that AWD 131-138 is effective in treating AGS and absence epilepsy, which is a form of idiopathic epilepsy.

It is noted that the claim limitation of "…said idiopathic epilepsy being characterized by excessive transient paroxysmal neuronal discharge in the cerebral cortex of said dog, when no underlying cause can be found via clinical and pathological

examination…" refers to the mechanism of action of the idiopathic epilepsy. If it is determined that the treatment will treat idiopathic epilepsy, then it will obviously treat idiopathic epilepsy, regardless of how it is characterized.

Claims 16-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bialer et al. (J Epilepsy Research (2001) 43, pgs. 11-58) in view of Ross et al. (Neurosci Biobehav Rev, 24 (2000) 639-653) and French (Am J Managed Care, Vol. 7, No. 7, 2001) as applied to claims 12-15 and 19 above, in view of Thomas (Veterinary Clinics of North America Small Animal Practice (2000), 30, pgs. 183-206).

Bialer et al. teach that AWD 131-138 treats idiopathic epilepsy in dog seizure models as described in the above rejection.

Bialer et al. does not teach the co-administration of another active ingredient.

Thomas et al. teach that Phenobarbital is the initial choice of treatment for idiopathic epilepsy in dogs (meeting the limitations of claims 16-17; pg. 191, Choice of Treatment).

It would be obvious to one having ordinary skill in the art at the time of the invention that AWD 131-138 would be successful in treating idiopathic epilepsy in dogs by the teachings of Bialer et al., which teach that AWD 131-138 is effective in treating animal-models of idiopathic epilepsy. Furthermore, it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose. The idea of combining them flows logically from their having been individually taught in the prior art. In re Kerkhoven, 626 F.2d 846, 205 USPQ 1069, 1072 (CCPA

1980). Therefore, it would be obvious to co-administer another active ingredient such as Phenobarbital because it is useful in the treatment of idiopathic epilepsies as taught by Thomas et al. One would be motivated to administer the combined treatment with a reasonable expectation of success because both AWD 131-138 and Phenobarbital are taught to effectively treat idiopathic epilepsy.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Renee Claytor whose telephone number is (571)272-8394. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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